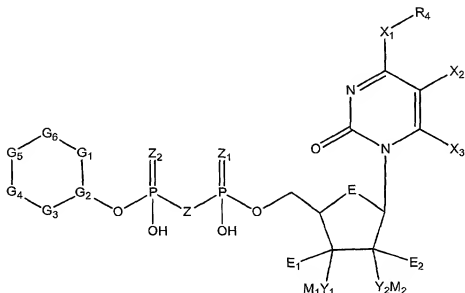


## WHAT IS CLAIMED:

1. A method of reducing intraocular pressure comprising administering to a subject a pharmaceutical composition comprising an effective amount of a compound of Formula I, its diastereomers, enantiomers, tautomers, or pharmaceutically acceptable salts thereof:



wherein:

- 10  $X_1 = O, NR, S, CF_2, CF_3$  or  $CN$  with the proviso that when  $X_1 = CF_3$  or  $CN$ , then  $R_4$  is absent; or  
 $X_1$  represents a bond from the pyrimidine ring to  $R_4$ ;  
 $X_2 = H, F, Cl, Br, I, CN, OR_8, SR_8, NR_9R_{13}, CF_3$ , alkyl, cycloalkyl, arylalkyl, aryl, arylalkenyl, arylalkynyl,  $C(O)R_{16}$ ,  $C(O)OR_{17}$ ,  $C(O)NR_{16}R_{18}$  or heterocycle of 5 to 7 members;
- 15  $X_3 = H, CN, OR_{19}, SR_{19}, NR_{23}R_{28}, CF_3$ , alkyl, cycloalkyl,  $C(O)R_{32}$ ,  $C(O)OR_{33}$ ,  $C(O)NR_{34}R_{35}$ , arylalkyl, aryl, arylalkenyl, arylalkynyl, or a heterocycle of 5 to 7 members;  
 $R = H, OR_1$ , alkyl, cycloalkyl, arylalkyl, aryl,  $C(O)R_2$ ,  $C(O)OR_3$  or  $C(O)NR_1R_2$ ;  
 $R_1, R_7, R_{10}, R_{22}, R_{24}, R_{27}, R_{31}, R_{33}$  and  $R_{35}$  are each independently  $H$ , alkyl, cycloalkyl, arylalkyl or aryl;
- 20  $R_2 = H$ , alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members; or  
 $R_1$  and  $R_2$  taken together can form a heterocyclic ring of 5 to 7 members;

R<sub>3</sub>, R<sub>6</sub>, R<sub>8</sub>, R<sub>12</sub>, R<sub>15</sub>, R<sub>17</sub>, R<sub>21</sub>, R<sub>26</sub> and R<sub>30</sub> are independently alkyl, cycloalkyl, arylalkyl or aryl;

R<sub>4</sub> = H, alkyl, cycloalkyl, arylalkyl, aryl, heterocyclic ring of 5 to 7 members, C(O)R<sub>5</sub>, C(O)OR<sub>6</sub> or C(O)NR<sub>5</sub>R<sub>7</sub>;

- 5 R<sub>5</sub>, R<sub>11</sub>, R<sub>14</sub>, R<sub>16</sub>, R<sub>18</sub>, R<sub>20</sub>, R<sub>25</sub>, R<sub>29</sub>, R<sub>32</sub> and R<sub>34</sub> are independently H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;

R<sub>9</sub> = H, OR<sub>10</sub>, alkyl, cycloalkyl, arylalkyl, aryl, C(O)R<sub>11</sub>, C(O)OR<sub>12</sub> or C(O)NR<sub>10</sub>R<sub>11</sub>;

R<sub>13</sub> = H, alkyl, cycloalkyl, arylalkyl, aryl, C(O)R<sub>14</sub> or C(O)OR<sub>15</sub>;

R<sub>19</sub> = alkyl, cycloalkyl, arylalkyl, or aryl, C(O)R<sub>20</sub>, C(O)OR<sub>21</sub> or C(O)NR<sub>20</sub>R<sub>22</sub>;

- 10 R<sub>23</sub> = H, OR<sub>24</sub>, alkyl, cycloalkyl, arylalkyl, aryl, C(O)R<sub>25</sub>, C(O)OR<sub>26</sub> or C(O)NR<sub>25</sub>R<sub>27</sub>;

where R<sub>26</sub> and R<sub>29</sub> taken together can form a heterocyclic ring of 6 or 7 members;

or R<sub>2</sub> and R<sub>4</sub>, R<sub>2</sub> and R<sub>5</sub>, R<sub>10</sub> and R<sub>11</sub>, R<sub>9</sub> and R<sub>13</sub>, R<sub>10</sub> and R<sub>13</sub>, R<sub>9</sub> and R<sub>14</sub>, R<sub>11</sub> and R<sub>14</sub>, R<sub>9</sub>

and R<sub>15</sub>, R<sub>11</sub> and R<sub>15</sub>, R<sub>16</sub> and R<sub>18</sub>, R<sub>20</sub> and R<sub>22</sub>, R<sub>25</sub> and R<sub>27</sub>, R<sub>23</sub> and R<sub>28</sub>, R<sub>24</sub> and R<sub>28</sub>, R<sub>25</sub> and

R<sub>28</sub>, R<sub>25</sub> and R<sub>29</sub>, R<sub>29</sub> and R<sub>31</sub> or R<sub>34</sub> and R<sub>35</sub> are optionally taken together to form a

- 15 heterocyclic ring of 5 to 7 members;

E = O or CH<sub>2</sub>;

E<sub>1</sub> and E<sub>2</sub> independently are H or F; or

E<sub>1</sub> and E<sub>2</sub>, when taken together, form a carbon-carbon bond;

Y<sub>1</sub> = O or F, with the proviso that when Y<sub>1</sub> = F, then M<sub>1</sub> is absent; or

- 20 Y<sub>1</sub> represents a bond from the point of ring attachment to M<sub>1</sub>;

Y<sub>2</sub> = O or F, with the proviso that when Y<sub>2</sub> = F, then M<sub>2</sub> is absent; or

Y<sub>2</sub> represents a bond from the point of ring attachment to M<sub>2</sub>;

M<sub>1</sub> and M<sub>2</sub> are independently H, alkyl, cycloalkyl, arylalkyl, aryl, C(O)M<sub>3</sub>, C(O)OM<sub>4</sub>, or C(O)NM<sub>3</sub>M<sub>5</sub>;

- 25 M<sub>3</sub> = H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;

M<sub>4</sub> = alkyl, cycloalkyl, arylalkyl or aryl;

M<sub>5</sub> = H, alkyl, cycloalkyl, arylalkyl, or aryl; or

M<sub>3</sub> and M<sub>5</sub> taken together form a heterocyclic ring of 5 to 7 members;

when Y<sub>1</sub> = Y<sub>2</sub> = O, M<sub>1</sub> and M<sub>2</sub> optionally are bonds from the oxygen atoms of Y<sub>1</sub> and Y<sub>2</sub>,

- 30 respectively, to a carbon atom of an acetal-, ketal- or orthoester group E<sub>3</sub>;

wherein E<sub>3</sub> is Q(A<sub>1</sub>)(A<sub>2</sub>);

wherein Q is a carbon atom;

A<sub>1</sub> = H, CF<sub>3</sub>, alkyl, cycloalkyl, arylalkyl or aryl;

$A_2 = \text{H, O}A_3, \text{CF}_3, \text{alkyl, cycloalkyl, arylalkyl, aryl or heterocycle of 5 to 7 members;}$

$A_3 = \text{alkyl, cycloalkyl, arylalkyl or aryl; or}$

where  $A_1$  and  $A_2$ , when taken together, form a carbocyclic ring of 5 or 6 members, with or without unsaturation, and with or without substitution; or

- 5  $M_1Q(A_1)(A_2)M_2$  is taken together to form a carbonyl bonded to  $Y_1$  and  $Y_2$ , such that a cyclic carbonate is formed;

$Z = \text{O, NZ}_3, \text{CH}_2, \text{CHF, CF}_2, \text{CCl}_2, \text{or CHCl};$

$Z_1$  and  $Z_2$  are independently O or S;

$Z_3 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or a heterocyclic ring of 5 to 7 members;}$

- 10  $G_1 = \text{O, S, CH}_2 \text{ or CH(OJ}_1\text{);}$

$G_2 = \text{CH, C(CH}_2\text{OJ}_3\text{), CCH}_3, \text{CCF}_3, \text{or C(CO}_2\text{J}_4\text{);}$

$G_3 = \text{CH}_2, \text{CHF, CF}_2, \text{CH(OJ}_5\text{) or CH(NJ}_6\text{J}_7\text{);}$

$G_4 = \text{CH}_2, \text{CHF, CF}_2, \text{CH(OJ}_9\text{), or CH(NJ}_{11}\text{J}_{13}\text{);}$

$G_5 = \text{CH}_2, \text{CHF, CF}_2, \text{CH(OJ}_{15}\text{), or CH(NJ}_{16}\text{J}_{17}\text{);}$

- 15  $G_6 = \text{CH}_2, \text{CH(CH}_3\text{), CH(CHF}_2\text{), CH(CF}_3\text{), CH(OJ}_{19}\text{), CH(CH}_2\text{OJ}_{19}\text{), CH(CH}_2\text{(NJ}_{21}\text{J}_{23}\text{))}, \text{or CH(CO}_2\text{J}_{22}\text{), with the provision that when } G_1 = \text{O or S, then } G_6 \text{ does not equal CH(OH); and the number of hydrogen atoms bonded to the } G_1\text{-}G_6 \text{ ring atoms is limited to a maximum of 8; also with the provision that the number of nitrogen atoms bonded to the } G_1\text{-}G_6 \text{ ring atoms in Formula I is limited to a maximum of 2;}$

- 20  $J_1 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, or C(O)J}_2\text{;}$

$J_2, J_6, J_8, J_{10}, J_{11}, J_{14}, J_{16}, J_{18}, J_{20}, J_{22}, \text{ and } J_{24}$  are independently H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;

$J_3 = \text{alkyl, cycloalkyl, arylalkyl, aryl or C(O)J}_2\text{;}$

$J_4 = \text{alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;}$

- 25  $J_5 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, or C(O)J}_6\text{;}$

$J_7 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J}_8\text{;}$

$J_9 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, C(O)J}_{10}, \text{CH(CH}_3\text{)(CO}_2\text{J}_{11}\text{), or}$

$\text{CH(CH}_3\text{)(C(O)NJ}_{11}\text{J}_{12}\text{);}$

- 30  $J_{12} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, heterocyclic ring of 5 to 7 members, an amino acid radical of 2 to 12 carbon atoms with or without hetero atoms, or a peptide radical comprising 2 to 10 amino acid units;}$

$J_{13} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J}_{14}\text{;}$

$J_{15} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or C(O)J}_{16}\text{;}$

$J_{17} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or } \text{C}(\text{O})J_{18};$

$J_{19} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or } \text{C}(\text{O})J_{20};$

$J_{21} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, } \text{C}(\text{O})J_{22} \text{ or heterocyclic ring of 5 to 7 members;}$

$J_{23} = \text{H, alkyl, cycloalkyl, arylalkyl, aryl or } \text{C}(\text{O})J_{24}; \text{ or}$

- 5  $J_6$  and  $J_7$ ,  $J_{11}$  and  $J_{12}$ ,  $J_{11}$  and  $J_{13}$ ,  $J_{16}$  and  $J_{17}$  or  $J_{21}$  and  $J_{23}$  are optionally taken together to form a heterocyclic ring of 5 to 7 members; or

where  $J_{22}$  and  $J_{24}$ , when taken together, form a heterocyclic ring of 5 to 7 members or a bicyclic imide comprising 4 to 12 carbons, with or without unsaturation and/or with or without substitution; or

- 10 when  $G_1 = \text{CH}(\text{O}J_1)$  and  $G_2 = \text{C}(\text{CH}_2\text{O}J_3)$ ,  $J_1$  and  $J_3$  optionally are bonds from the oxygen atoms of  $G_1$  and  $G_2$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group  $G_7$ ; wherein

$G_7 = \text{Q}_1(\text{T}_1)(\text{T}_2); \text{ or}$

- 15 when  $G_2 = \text{C}(\text{CH}_2\text{O}J_5)$  and  $G_3 = \text{CH}(\text{O}J_5)$ ,  $J_3$  and  $J_5$  optionally are bonds from the oxygen atoms of  $G_2$  and  $G_3$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group  $G_8$ ; wherein

$G_8 = \text{Q}_1(\text{T}_1)(\text{T}_2); \text{ or}$

when  $G_3 = \text{CH}(\text{O}J_5)$  and  $G_4 = \text{C}(\text{CHO}J_9)$ ,  $J_5$  and  $J_9$  optionally are bonds from the oxygen atoms of  $G_3$  and  $G_4$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group

- 20  $G_9$ ; wherein

$G_9 = \text{Q}_1(\text{T}_1)(\text{T}_2); \text{ or}$

when  $G_4 = \text{C}(\text{CHO}J_9)$  and  $G_5 = \text{CH}(\text{O}J_{15})$ ,  $J_9$  and  $J_{15}$  optionally are bonds from the oxygen atoms of  $G_4$  and  $G_5$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group  $G_{10}$ ; wherein

- 25  $G_{10} = \text{Q}_1(\text{T}_1)(\text{T}_2); \text{ or}$

when  $G_5 = \text{C}(\text{CHO}J_{15})$  and  $G_6 = \text{CHCH}_2(\text{O}J_{19})$ ,  $J_{15}$  and  $J_{19}$  optionally are bonds from the oxygen atoms of  $G_5$  and  $G_6$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group  $G_{11}$ ;

wherein  $G_{11} = \text{Q}_1(\text{T}_1)(\text{T}_2); \text{ or}$

- 30 when  $G_1 = \text{CH}(\text{O}J_1)$  and  $G_6 = \text{CH}(\text{CH}_2\text{O}J_{19})$  or  $\text{CH}(\text{O}J_{19})$ ,  $J_1$  and  $J_{19}$  are optionally bonds from the oxygen atoms of  $G_1$  and  $G_6$ , respectively, to a carbon atom of an acetal-, ketal- or orthoester group  $G_{12}$ ;

wherein  $G_{12} = \text{Q}_1(\text{T}_1)(\text{T}_2);$

wherein Q<sub>1</sub> is a carbon atom; and

T<sub>1</sub> = H, CF<sub>3</sub>, alkyl, cycloalkyl, arylalkyl or aryl;

T<sub>2</sub> = H, OT<sub>3</sub>, CF<sub>3</sub>, alkyl, cycloalkyl, arylalkyl, aryl or heterocycle of 5 to 7 members;

T<sub>3</sub> = alkyl, cycloalkyl, arylalkyl or aryl; or

- 5 T<sub>1</sub> and T<sub>2</sub>, when taken together, form a carbocyclic ring of 5 or 6 members, with or without unsaturation and with or without substitution; or  
Q<sub>1</sub>(T<sub>1</sub>)(T<sub>2</sub>) is taken together to form a carbonyl, such that a cyclic carbonate is formed.

2. The method according to Claim 1, wherein:

- 10 X<sub>1</sub> = O, NR, S; or

X<sub>1</sub> represents a bond from the pyrimidine ring to R<sub>4</sub>;

X<sub>2</sub> = H, F, Cl, Br, I, CF<sub>3</sub>, alkyl, cycloalkyl, arylalkyl, aryl, arylalkenyl, arylalkynyl,

C(O)OR<sub>17</sub>, C(O)NR<sub>16</sub>R<sub>18</sub> or heterocycle of 5 to 7 members;

X<sub>3</sub> = H, CN, C(O)OR<sub>33</sub>;

- 15 R = H, alkyl, cycloalkyl, arylalkyl, aryl;

Y<sub>1</sub> = O; or

Y<sub>1</sub> represents a bond from the point of ring attachment to M<sub>1</sub>;

Y<sub>2</sub> = O; or

Y<sub>2</sub> represents a bond from the point of ring attachment to M<sub>2</sub>;

- 20 M<sub>3</sub> = alkyl, cycloalkyl, arylalkyl, or aryl;

M<sub>4</sub> = alkyl, cycloalkyl, arylalkyl or aryl;

A<sub>1</sub> = H, alkyl, cycloalkyl, arylalkyl or aryl;

A<sub>2</sub> = H, alkyl, cycloalkyl, arylalkyl, aryl or heterocycle of 5 to 7 members; or

where A<sub>1</sub> and A<sub>2</sub>, when taken together, form a carbocyclic ring of 5 or 6 members, with or

- 25 without unsaturation, and with or without substitution; or

M<sub>1</sub>Q(A<sub>1</sub>)(A<sub>2</sub>)M<sub>2</sub> is taken together to form a carbonyl bonded to Y<sub>1</sub> and Y<sub>2</sub>, such that a cyclic carbonate is formed;

Z = O, CH<sub>2</sub>, CF<sub>2</sub>, or CCl<sub>2</sub>;

G<sub>2</sub> = CH, C(CH<sub>2</sub>OJ<sub>3</sub>), or C(CO<sub>2</sub>J<sub>4</sub>);

- 30 J<sub>3</sub> = alkyl or C(O)J<sub>2</sub>;

J<sub>4</sub> = alkyl;

J<sub>5</sub> = H, alkyl or C(O)J<sub>6</sub>;

J<sub>7</sub> = H, or alkyl;

- $J_9 = \text{H, alkyl or C(O)J}_{10}$ ;  
 $J_{13} = \text{H, alkyl, or C(O)J}_{14}$ ;  
 $J_{15} = \text{H, alkyl, or C(O)J}_{16}$ ;  
 $J_{17} = \text{H, alkyl, or C(O)J}_{18}$ ;  
5  $J_{21} = \text{H, alkyl, C(O)J}_{22}$  or heterocyclic ring of 5 to 7 members;  
 $T_1 = \text{H, alkyl, or arylalkyl}$ ;  
 $T_2 = \text{H, alkyl, arylalkyl, or heterocycle of 5 to 7 members}$ ; or  
 $T_1$  and  $T_2$ , when taken together, form a carbocyclic ring of 5 or 6 members, with or without unsaturation and with or without substitution; or  
10  $Q_1(T_1)(T_2)$  is taken together to form a carbonyl, such that a cyclic carbonate is formed.

3. The method according to Claim 2, wherein:  
 $X_1 = \text{O, NR, S}$ ;  
15  $X_2 = \text{H, F, Cl, Br, I, CF}_3$ , alkyl, arylalkyl, aryl, arylalkenyl, arylalkynyl, or heterocycle of 5 to 7 members;  
 $X_3 = \text{H}$ ;  
 $R = \text{H, alkyl, cycloalkyl, arylalkyl, aryl}$ ;  
 $R_4 = \text{H, alkyl, cycloalkyl, arylalkyl, aryl, or C(O)R}_5$ ;  
20  $R_5$  is H, alkyl, cycloalkyl, arylalkyl, aryl or heterocyclic ring of 5 to 7 members;  
 $E_1$  and  $E_2$  are H;  
 $Y_1 = \text{O}$ ;  
 $Y_2 = \text{O}$ ;  
 $M_1$  and  $M_2$  are independently H, alkyl, cycloalkyl, arylalkyl, aryl, C(O) $M_3$ ;;  
25  $M_3 = \text{alkyl, cycloalkyl, arylalkyl, or aryl}$ ;  
 $A_1 = \text{H, alkyl, cycloalkyl, arylalkyl or aryl}$ ;  
 $A_2 = \text{H, alkyl, cycloalkyl, arylalkyl, or aryl}$ ;  
 $Z = \text{O, CH}_2$ ,  $\text{CF}_2$ , or  $\text{CCl}_2$ ;  
 $G_1 = \text{O or S}$ ;  
30  $G_2 = \text{CH}$ ;  
 $G_3 = \text{CH}_2$ ,  $\text{CH(OJ}_5)$  or  $\text{CH(NJ}_6\text{J}_7)$ ;  
 $G_4 = \text{CH}_2$ ,  $\text{CH(OJ}_9)$ , or  $\text{CH(NJ}_{11}\text{J}_{13})$ ;  
 $G_5 = \text{CH}_2$ ,  $\text{CH(OJ}_{15})$ , or  $\text{CH(NJ}_{16}\text{J}_{17})$ ;

$G_6 = CH_2, CH(CH_3), CH(OJ_{19}), CH(CH_2OJ_{19}), CH(CH_2(NJ_{21}J_{23})),$  or  $CH(CO_2J_{21}),$  with the provision that when  $G_1 = O$  or  $S,$  then  $G_6$  does not equal  $CH(OH);$  and the number of hydrogen atoms bonded to the  $G_1$ - $G_6$  ring atoms is limited to a maximum of 8; also with the provision that the number of nitrogen atoms bonded to the  $G_1$ - $G_6$  ring atoms in

5 Formula I is limited to a maximum of 2;

$J_6, J_{11},$  and  $J_{16}$  are independently  $H,$  alkyl, arylalkyl, or aryl;

$J_5 = H,$  alkyl or  $C(O)J_6;$

$J_7 = H,$  or alkyl;

$J_9 = H,$  alkyl or  $C(O)J_{10};$

10  $J_{13} = H,$  alkyl, or  $C(O)J_{14};$

$J_{15} = H,$  alkyl, or  $C(O)J_{16};$

$J_{17} = H,$  alkyl, or  $C(O)J_{18};$

$J_{19} = H,$  alkyl, or  $C(O)J_{20};$

$J_{21} = H,$  alkyl, or  $C(O)J_{22};$  and

15  $J_{23} = H,$  alkyl, or  $C(O)J_{24}.$

4. The method according to Claim 1, wherein said method further comprises the step of measuring the intraocular pressure of said subject before administering the composition.

20 5. The method according to Claim 1, further comprising the step of measuring the intraocular pressure of said subject after administering the composition.

6. The method according to Claim 1, wherein administering said pharmaceutical composition to said subject is to treat ocular hypertension.

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7. The method according to Claim 6, wherein administering said pharmaceutical composition to said subject is to treat glaucoma.

8. The method according Claim 1, wherein said pharmaceutical composition is co-administered to said subject with other therapeutic agent or adjuvant therapy commonly used to reduce intraocular pressure.

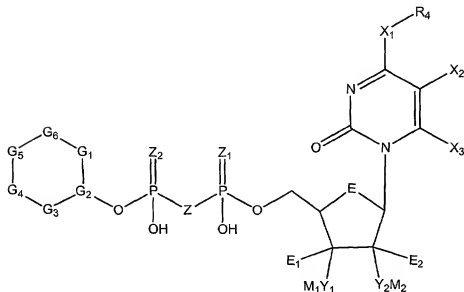
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9. The method according to Claim 1, wherein said pharmaceutical composition is administered topically to said subject.

10. The method according to Claim 1, wherein said pharmaceutical composition is administered via subconjunctival, subcleral, or intravitreal injection to said subject.

11. A compound according to Formula IA:

**Formula IA**



wherein:

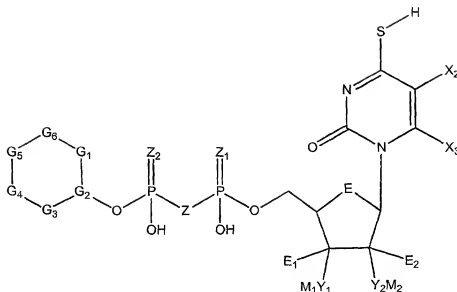
$R_4$  = alkyl, cycloalkyl, arylalkyl, aryl, heterocyclic ring of 5 to 7 members,  $C(O)R_5$ ,  $C(O)OR_6$  or  $C(O)NR_5R_7$ ;

15  $X_1$ ,  $X_2$ ,  $X_3$ ,  $R$ ,  $R_1-R_3$ ,  $R_5-R_{35}$ ,  $E$ ,  $E_1$ ,  $E_2$ ,  $Y_1$ ,  $Y_2$ ,  $M_1-M_5$ ,  $A_1-A_3$ ,  $Z$ ,  $Z_1-Z_3$ ,  $G_1-G_6$ ,  $J_1-J_{24}$ ,  $G_1-G_{12}$ ,  $T_1-T_3$  are the same as those described in Formula I in Claim 1.



12. A compound of Formula IB:

Formula IB



5 wherein:

$X_2, X_3, R, R_1-R_3, R_5-R_{35}, E, E_1, E_2, Y_1, Y_2, M_1-M_5, A_1-A_3, Z, Z_1-Z_3, G_1-G_6, J_1-J_{24}, G_1-G_{12}, T_1-T_3$  are the same as those described in Formula I in Claim 1;

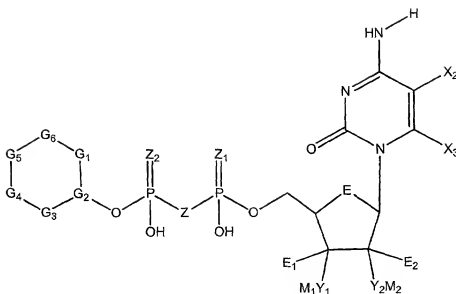
provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O, E_1 = E_2 = H,$

$G_2 = CH, G_3 = CH(OJ_5), G_4 = CH(OJ_9), G_5 = CH(OJ_{15})$  and  $G_6 = CH(CH_2OJ_{19}),$  then at least

10 one of  $X_2, X_3, M_1, M_2, J_5, J_9, J_{15},$  or  $J_{19}$  is not equal to H.

13. A compound of Formula IC:

Formula IC:



5

wherein

$X_2, X_3, R, R_1-R_3, R_5-R_{35}, E, E_1, E_2, Y_1, Y_2, M_1-M_5, A_1-A_3, Z, Z_1-Z_3, G_1-G_6, J_1-J_{24}, G_1-G_{12}, T_1-T_3$  are the same as those described in Formula I in Claim 1;

provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = O, G_1 = O$  or  $CH(OH), E_1 = E_2 = H, G_2 =$

- 10  $CH, G_3 = CH(OJ_5), G_4 = CH(OJ_9), G_5 = CH(OJ_{15})$  and  $G_6 = CH(CH_2OJ_{19})$ , then at least one of  $X_2, X_3, M_1, M_2, J_5, J_9, J_{15}$ , or  $J_{19}$  is not equal to H;

further provided that when  $X_2 = H$  or  $CH_2OH, E = Y_1 = Z = Z_1 = Z_2 = G_1 = O, Y_2 =$  bond to  $M_2$  from ring,  $E_1 = E_2 = M_2 = H, G_2 = CH, G_3 = CH(OJ_5)$  and  $G_4 = CH(OJ_9), G_5 = CH(OJ_{15}), G_6 = CH(CH_2OJ_{19})$ , then at least one of  $X_3, M_1, J_5, J_9, J_{15}$ , or  $J_{19}$  is not equal to H;

- 15 further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O, E_1 = E_2 = H, G_2 = CH, G_3 = CH(OJ_5), G_4 = CH_2, G_5 = CH(OJ_{15}), G_6 = CH(CH_3)$ , then at least one of  $X_2, X_3, M_1, M_2, J_5$ , or  $J_{15}$  is not equal to H;

further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O, E_1 = E_2 = H, G_2 = CH, G_3 = CH_2$  or  $CH(NH_2), G_4 = CH(OJ_9), G_5 = CH(OJ_{15}), G_6 = CH(CH_3)$ , then at least one of  $X_2, X_3,$

- 20  $M_1, M_2, J_9$ , or  $J_{15}$  is not equal to H;

further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O$ ,  $E_1 = E_2 = H$ ,  $G_2 = CH$ ,  $G_3 = CH(NH_2)$ ,  $G_4 = CH(OJ_9)$ ,  $G_5 = CH(OJ_{15})$ ,  $G_6 = CH(CH_2(NH_2))$ , then at least one of  $X_2$ ,  $X_3$ ,  $M_1$ ,  $M_2$ ,  $J_9$ , or  $J_{15}$  is not equal to H;

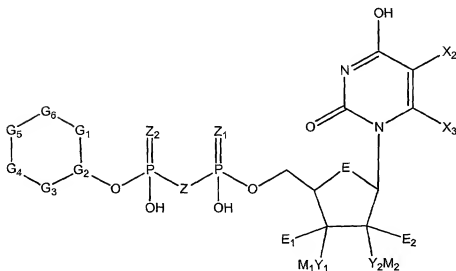
further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O$ ,  $E_1 = E_2 = H$ ,  $G_2 = CH$ ,  $G_3 = CH(OH)$ ,  $G_4 = CH_2$ ,  $G_6 = CH(CH_3)$ , then  $G_5$  is not equal to CHF;

further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O$ ,  $E_1 = E_2 = X_2 = X_3 = M_1 = M_2 = H$ ,  $G_2 = CH$ ,  $G_3 = CH(OH)$ ,  $G_4 = CH(OH)$ ,  $G_5 = CH(OH)$ , then  $G_6$  is not  $CH(CH_3)$  or  $CH(CHF_2)$ ;

further provided that when  $E = Y_1 = Y_2 = Z = Z_1 = Z_2 = G_1 = O$ ,  $E_1 = E_2 = H$ ,  $G_2 = CH$ ,  $G_3 = CH(OH)$ ,  $G_5 = CH(OH)$ ,  $G_6 = CH(CH_2OH)$  then  $G_4$  is not CHF.

14. A compound of Formula ID:

#### Formula ID



wherein:

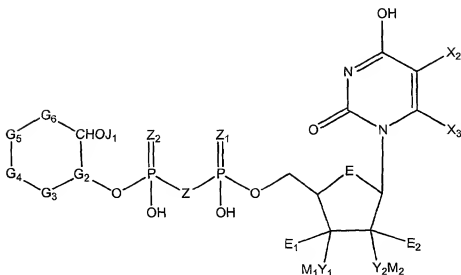
$X_3 = CN$ ,  $OR_{19}$ ,  $SR_{19}$ ,  $NR_{23}R_{28}$ ,  $CF_3$ , alkyl, cycloalkyl,  $C(O)R_{32}$ ,  $C(O)OR_{33}$ ,  $C(O)NR_{34}R_{35}$ , arylalkyl, aryl, arylalkenyl, arylalkynyl, or a heterocycle of 5 to 7 members;

X<sub>2</sub>, X<sub>3</sub>, E, E<sub>1</sub>, E<sub>2</sub>, Y<sub>1</sub>, Y<sub>2</sub>, M<sub>1</sub>, M<sub>2</sub>, Z, Z<sub>1</sub>, Z<sub>2</sub>, and G<sub>1</sub>-G<sub>6</sub> are the same as those described in Formula I in Claim 1.

15. A compound of Formula IE:

5

Formula IE



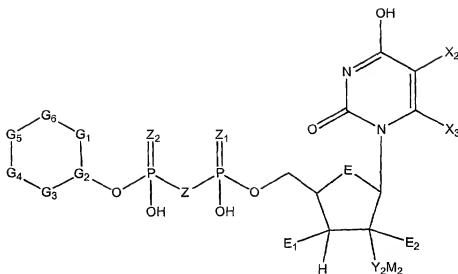
wherein:

X<sub>2</sub>, X<sub>3</sub>, E<sub>1</sub>, E<sub>2</sub>, Y<sub>1</sub>, Y<sub>2</sub>, M<sub>1</sub>, M<sub>2</sub>, Z, Z<sub>1</sub>, Z<sub>2</sub>, G<sub>2</sub>-G<sub>6</sub> and J<sub>1</sub> are the same as those described in Formula I in Claim 1.

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16. A compound of Formula IF:

Formula IF



5 wherein:

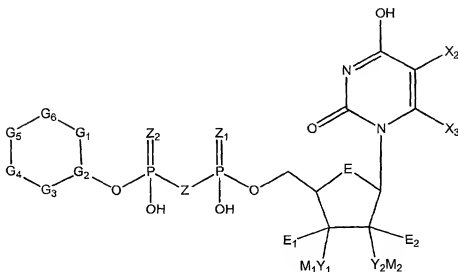
$X_2, X_3, E_1, E_2, Y_2, M_2, Z, Z_1, Z_2, G_2-G_6$  are the same as those described in Formula I;

Provided that when  $X_2 = CH_3, X_3 = E_1 = E_2 = M_2 = H, E = Y_2 = Z = Z_1 = Z_2 = G_1 = O, G_2 =$

$CH, G_3 = G_4 = G_5 = CH(OH)$ , then  $G_6$  is not  $CH(CH_3)$  or  $CH(CH_3)$  or  $CH(CH_2OH)$ .

10

Formula IG



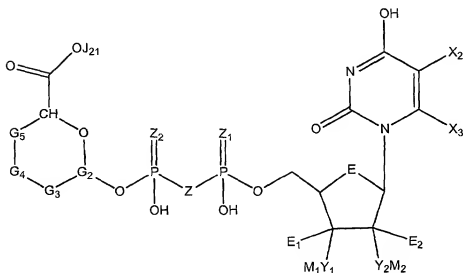
wherein:

X<sub>2</sub> is aryl, arylalkyl, arylalkenyl, arylalkynyl, C<sub>2</sub>-C<sub>8</sub> alkyl, C<sub>2</sub>-C<sub>8</sub> alkenyl, alkynyl, cycloalkyl, or C<sub>3</sub>-C<sub>8</sub> branched alkyl, and none of the alkyl groups in X<sub>2</sub> are substituted with an amine or an amide on the chain, or contain a nitrogen hetero atom;

X<sub>3</sub>, E<sub>1</sub>, E<sub>2</sub>, M<sub>1</sub>, M<sub>2</sub>, Y<sub>1</sub>, Y<sub>2</sub>, Z, Z<sub>1</sub>, Z<sub>2</sub>, G<sub>1</sub>-G<sub>6</sub> are the same as those described in Formula I in Claim 1.

17. A compound of Formula IH:

Formula IH

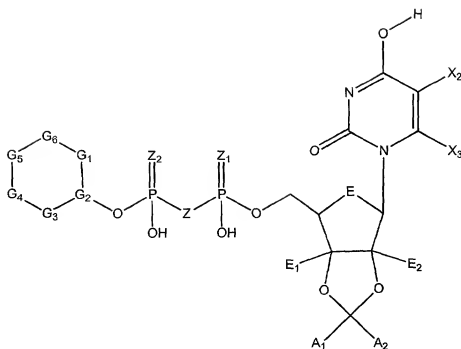


wherein:

- 15 X<sub>2</sub>, X<sub>3</sub>, E, E<sub>1</sub>, E<sub>2</sub>, M<sub>1</sub>, M<sub>2</sub>, Y<sub>1</sub>, Y<sub>2</sub>, Z, Z<sub>1</sub>, Z<sub>2</sub>, G<sub>2</sub>-G<sub>5</sub> and J<sub>21</sub> are the same as those described in Formula I in Claim 1;  
provided that when X<sub>2</sub> = X<sub>3</sub> = E<sub>1</sub> = E<sub>2</sub> = M<sub>1</sub> = M<sub>2</sub> = H, E = Y<sub>1</sub> = Y<sub>2</sub> = Z = Z<sub>1</sub> = Z<sub>2</sub> = O, G<sub>2</sub> = CH, G<sub>3</sub> = G<sub>4</sub> = G<sub>5</sub> = CH(OH), then J<sub>21</sub> is not H or CH<sub>3</sub>.

18 A compound of Formula II:

Formula II



5

wherein:

$X_2$ ,  $X_3$ , E,  $E_1$ ,  $E_2$ ,  $A_1$ ,  $A_2$ , Z,  $Z_1$ ,  $Z_2$  and  $G_2$ - $G_6$  are the same as those described in Formula I in Claim 1;

provided that when  $X_2 = X_3 = E_1 = E_2 = H$ , and  $E = Z_1 = Z_2 = G_1 = O$ , and  $A_1 = A_2 = CH_3$ ,

10 then Z is not equal to  $CH_2$  or  $CF_2$ ;

further provided that when  $X_2 = X_3 = E_1 = E_2 = H$ , and  $E = Z = Z_1 = Z_2 = G_1 = O$ , and  $A_1$  and  $A_2$  are taken together to form an unsaturated 6-membered ring, then  $G_6$  is not  $CH(CH_2OH)$ .

15